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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,497	02/17/2000	DAVID J. FITZGERALD	015280-317100US	4036
7590	08/11/2004		EXAMINER	
JOHN STORELLA TOWNSEND AND TOWNSEND AND CREW TWO EMBARCADERO CENTER 8TH FLOOR SAN FRANCISCO, CA 94111-3834			HELMS, LARRY RONALD	
			ART UNIT	PAPER NUMBER
			1642	
			DATE MAILED: 08/11/2004	

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)
	09/381,497	FITZGERALD
	Examiner	Art Unit
	Larry R. Helms	1642

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 July 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) The period for reply expires 3 months from the mailing date of the final rejection.
 b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
 2. The proposed amendment(s) will not be entered because:
 (a) they raise new issues that would require further consideration and/or search (see NOTE below);
 (b) they raise the issue of new matter (see Note below);
 (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. Applicant's reply has overcome the following rejection(s): none.
 4. Newly proposed or amended claim(s) ____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
 6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
 7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none.

Claim(s) objected to: none.

Claim(s) rejected: 1-4,7-11,13,14,16,17,22-26 and 29-32.

Claim(s) withdrawn from consideration: _____.

8. The drawing correction filed on ____ is a) approved or b) disapproved by the Examiner.
 9. Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
 10. Other: _____.



**LARRY R. HELMS, PH.D.
PRIMARY EXAMINER**

Continuation of 5. does NOT place the application in condition for allowance because: The declaration of Dr. Fitzgerald has been carefully considered but is deemed not to be persuasive. The declaration states that previous LL2-PE38 immunoconjugates were poorly cytotoxic and did not express well which is in contrast to the RFB4 conjugate and the high level of expression, retention of binding, suppperior toxicity of the RFB4ds(FV)-PE38 is suprising and can not be predicted from the art. In response to this argument, as stated previously the art did recognize dsFv as superior and Reiter et al (Nature Biotech) teach 4 out of 8 dsFv-immunotoxins had improved binding affinity (see page 1243, left column). The Reiter et al (Biochemistry) clearly shows better cytotoxicity for the dsFv as compared to the scFv and better expression yeilds (see Table 1) and better stability (see Table 2) and teach "that dsFv's have at least the same bindin properties as scFv's, and in some cases they may be better" (see abstract) and Reiter et al teach that scFv can retain the specificity and affinity of IgG (see page 5451). In addition, because the dsFv have suppperior charicteristics over the scFv they would obviously be chosen over scFv and in addition Shen et al teach that the Fab'-RFB4 bound 1.2 to 3.5 times more stronger than other Fab' fragments an the potent cytotoxic activity of the RFB4-AS appears to derive from their suppperior binding affinity and the art recognizes the suppperiority of this antibody. With regard to the Krietman et al reference, this reference demonstrates only one instant where the dsFv had low activity however, in all of Reiter et al (Biochemistry) and Kuan et al (Biochemistry) the dsFv were active and potent and as such one skill in the ar would have a reasonable expectation of success in making the claimed immunoconjugate dsFv with the RFB4 antibody. .



LARRY R. HELMS, PH.D.
PRIMARY EXAMINER